Withdrawal of Certain Rejections

Applicants gratefully acknowledge the withdrawal of the objection to the title, as well as the provisional rejection of claims 2, 6, 14-15, and 20 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-10, 16-21, 78-79, 81, 84, 86-88, 95, 97-98 and 100-104 of copending of USSN 10/163,657 in view of Ogilvie *et al.*, Salfeld *et al.*, and Smith *et al.*

Rejection of Claims 1, 3, 4, 12, 18, 22, 23, and 26-48 Under 35 USC § 103(a)

The Examiner has rejected claims 1, 3, 4, 12, 18, 22, 23, and 26-56 under 35 USC 103(a) as allegedly being unpatentable over Ogilvie *et al.* (British Journal of Dermatology, 144(3):587-589, March 2001) in view of Salfeld *et al.* ([a] WO 97/29131 or [b] U.S. 6,509,015), Smith *et al.* (Arthritis Rheum. 23(8):961-962, August 1980) and Keystone *et al.* (The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (The ARMADA Trial), *Presented at the Annual Meeting of the European League Against Rheumatoid Arthritis (EULAR), Prage, Czech Republic, 2001).* In particular, the Examiner indicates that it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to arrive at a method of treating psoriatic arthritis in a human patient comprising biweekly, subcutaneous administration of the D2E7 anti-TNFα antibody or fragments thereof at a dosage of 20 mg, 40 mg or 80 mg, in view of the combined teachings of these references. Applicants respectfully traverse this rejection.

The pending claims each require *subcutaneous* administration of a dosage comprising *10-150 mg* of a *human anti-TNFα antibody, or an antigen-binding fragment thereof*, whereby the dosage of the antibody, or antigen binding portion thereof, *is the same dosage throughout the course of treatment* for the treatment of *psoriatic arthritis (PsA)* or inhibition of human TNFα activity in a subject suffering from PsA. In addition, pending claims 1, 3, 12, 18, 22, 23, 26-53 further require *biweekly* administration of the human anti-TNFα antibody, or an antigen-binding fragment thereof.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference or to combine reference

teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). MPEP 706.02(j). The test for *prima facie* obviousness is consistent with the legal principles enunciated in *KSR Int'l Co. v. Teleflex Inc.,* 127 S. Ct. 1727 (2007). *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.,* 492 F.3d 1350, 1356 (Fed. Cir. 2007). The Examiner further notes that, "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense." *KSR*, 550 U.S. at ___, 82 USPQ2d at 1397 (see page 7 of Office Action).

The Examiner appears to be suggesting that the claimed invention would have been obvious to try based on the cited references. As described in MPEP § 2143 (E), to reject a claim based on this rationale, the Examiner must resolve the *Graham* factual inquiries, and subsequently establish a finding that at the time of the invention, there had been a recognized problem or need in the art; a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem; a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and whatever additional findings based on the *Graham* factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness based on the aforementioned rationale.

The primary reference relied upon by the Examiner is Ogilvie *et al.*, which reports improvements in PASI scores in six patients having psoriatic arthritis following infusion administration of the chimeric monoclonal anti-TNFα antibody infliximab at a weight-based dosage of 5 mg/kg at weeks 0, 2 and 6. Ogilvie *et al.* does not teach or suggest subcutaneous administration of a human TNFα antibody, or antigen-binding portion thereof, at a dosage comprising 10-150 mg, where the dosage is the same dosage throughout the course of treatment. To make up for these deficiencies, the Examiner combines the teachings of Ogilvie *et al.* with Salfeld *et al.*, Smith, and Keystone *et al.* Salfeld *et al.* describes functional human TNFα

antibodies, and Keystone describes results of a clinical trial for rheumatoid arthritis using D2E7, a human TNFα antibody. Smith is cited for teaching use of ibuprofen to treat PsA.

Applicants respectfully submit that the Examiner has failed to establish how the claimed methods were selected from a finite number of identified, predictable solutions, as required under the guidelines set forth under MPEP § 2143 (E) for establishing obviousness under the "obvious to try" rationale. Dosage amounts alone or in combination with a dosing schedule provide an infinite number of possible combinations for treatment. There exists a limitless number of dosage amounts that can be used in any given treatment, as there also exists a limitless dosing schedule in terms of how frequently an agent may be delivered. Accordingly, the combination of dose amounts and frequency is equally infinite, and does not represent a finite number of identified, predictable potential solutions to the allegedly recognized need or problem.

The Examiner is of the opinion that one of ordinary skill would look to Keystone *et al.* (directed to rheumatoid arthritis treatment) for guidance regarding treatment of psoriatic arthritis because "one of ordinary skill in the art would have a reasonable expectation of success in view of the teachings of Ogilvie *et al.* providing evidence that the administration of an anti-TNFα antibody is a clinically effective treatment for [psoriatic arthritis] and the fully human anti-TNFα antibody D2E7 was tolerated and therapeutically effective in patients according to Keystone *et al.*" Keystone *et al.* is specifically cited as teaching the fixed dose and subcutaneous administration described in the claims, as well as the dosing schedule described in claims 1, 3, 12, 18, 22, 23, 26-53. Applicants disagree and respectfully submit that one of ordinary skill in the art would not combine the teachings of Keystone *et al.* with Ogilvie *et al.* to arrive at the claimed invention. As described above, Ogilvie *et al.* teaches successful treatment of PsA. Applicants submit that based on the *successful* teachings of Ogilvie *et al.* regarding *infusion based* administration of infliximab using a *weight-based* dosing scheme, one of ordinary skill in the art would not be led to the claimed method of *subcutaneous* administration of a *fixed dose* (*i.e.,* the same dosage throughout the course of treatment). Even assuming *in arguendo* that one of ordinary skill would be motivated to substitute a human anti-TNFα antibody, or antigen-binding fragment thereof, for infliximab for treating psoriatic arthritis based on the teachings of Ogilvie *et al.* (which Applicants deny), the Examiner has not supported why one of ordinary skill would have changed the regimen described in Ogilvie *et al.* Given the successful treatment

described in Ogilvie *et al.*, Applicants submit that one of ordinary skill would have logically followed the *intravenous* and *weight-based* dosing scheme described in Ogilvie *et al.*, rather than modify the treatment method described therein.

The Examiner further suggests that the claimed invention is an optimization of the prior art, and, therefore, is obvious, citing *In re Aller*, 220 F.2d 454, 456 (see also MPEP 2144.05). Applicants respectfully note that the comparison of the claimed invention to the facts of *In re Aller* is not on point, as the claimed invention is not a mere optimization of a known process. The invention at issue in *In re Aller* was a process which was "identical with that of the prior art" except for the alteration of a temperature and ingredient concentration amount (*In re Aller*, 220 F.2d 454). The court held in *In re Aller* that the "claimed process [was] merely different in degree and not in kind from the reference process," and maintained the claimed invention as obvious over the cited reference.

Applicants' invention is based on the discovery that a human TNFα antibody, or antigen-binding portion thereof, may be used to treat PsA via subcutaneous administration to a subject in need thereof, as a fixed dose amount. The primary reference, Ogilvie *et al.*, teaches the use of a chimeric antibody via infusion at a weight-based dose of 5 mg/kg. Taking the method of Ogilvie *et al.* as the "known process" to which the Examiner is comparing Applicants' invention, the claimed invention is *not* an optimization of the parameters described in the cited reference, as the methods of treatment of the claimed invention and Ogilvie *et al.* share a common disease (PsA), but differ in the type of treatment (fixed dose vs. weight-based dosing), the type of therapeutic agent (human vs. chimeric TNFα antibody), and the mode of administration (subcutaneous vs. infusion). Moreover, claims 1, 3, 12, 18, 22, 23, 26-53 also differ in the dosing schedule in comparison to Ogilvie *et al.* Indeed, the Examiner relies upon three other references to make up for these deficiencies, including Keystone *et al.* for teaching a fixed dose. As such, *In re Aller* does not support the Examiner's position that the claimed invention is an optimization of a known process, *i.e.*, the method of Ogilvie *et al.*

In sum, Applicants respectfully submit that the claimed invention is not "obvious to try," as the invention was not derived from a finite number of possible combinations. In addition, the Examiner has failed to set forth why one of ordinary skill would look beyond the successful teachings of the primary reference to arrive at the claimed invention. Finally, the claimed

invention is inventive, as it is not an optimization of a known process as described under *In re Aller* cited by the Examiner.

In view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1, 3, 4, 12, 18, 22, 23, and 26-56 on Ground of Non-Statutory Obviousness-Type Double Patenting

The Examiner has rejected claims 1, 3-4, 12, 18, 22-23 and 26-56 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-7, 36-39 and 69 of U.S. Patent No. 6,509,015 (Salfeld *et al.* [b], described above) in view of Ogilvie *et al.*, Smith *et al.,* and Keystone *et al.* (described above). Applicants traverse this rejection.

As argued above, the Examiner has failed to establish a *prima facie* case of obviousness based on the combined teachings of Salfeld *et al.* alone or in combination with Ogilvie *et al.*, Smith, and Keystone *et al.* The claimed invention is not derived from a finite number of possible combinations described in the art, and is also not an optimization of a known process. Furthermore, there is no motivation to combine the cited references or modify the primary reference given the successful teachings of Ogilvie *et al.* Accordingly, Applicants respectfully request that the rejection of the pending claims on the ground of obviousness be reconsidered and withdrawn.

Provisional Rejection of Claims 1, 3, 4, 12, 18, 22-23, and 26-56 on the Ground of Nonstatutory Obviousness-Type Double Patenting

The *provisional* rejection of claims 1, 3, 4, 12, 18, 22-23, and 26-56 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-10, 16-21, 78-79, 81, 84, 86-88, 95, 97-98 and 100-104 of copending Application No. 10/163,657 in view of Ogilvie *et al.*, Salfeld *et al.* [a] and Smith *et al.* was maintained. In addition, the Examiner has *provisionally* rejected claims 1, 3, 4, 12, 18, 22, 23 and 26-56 as being unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 1, 4, 5, 8-11, 14, 38, 39, 49, 50, 52, 53 and 55-57 of copending Application No. 11/435,844 in view of Ogilvie *et al.*, Smith *et al.*, and Keystone *et al.* The Examiner has also *provisionally* rejected

claims 1, 3, 4, 12, 18, 22, 23 and 26-56 as being unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 15, 19, 56, 66, 77, and 87 of copending Application No. 11/233,252 in view of Ogilvie *et al.*, Salfeld *et al* (a), and Smith *et al.*

Applicants note that the foregoing rejections are *provisional* in nature and respectfully submit that they will be further addressed when appropriate, *i.e.*, when the nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the later-filed application (MPEP § 804 I.B.).

If a telephone conversation with Applicant's attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicant's attorney at (617) 227-7400.

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